



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/716,293

11/17/2003

Stephen P. Massia

049954-004100

8809

22204

7590

12/28/2010

NIXON PEABODY, LLP

401 9TH STREET, NW

SUITE 900

WASHINGTON, DC 20004-2128

EXAMINER

NIEBAUER, RONALD T

ART UNIT

PAPER NUMBER

1654

MAIL DATE

DELIVERY MODE

12/28/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/716,293	<b>Applicant(s)</b> MASSIA ET AL.	
	<b>Examiner</b> RONALD T. NIEBAUER	<b>Art Unit</b> 1654	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 16 November 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 102, 105 and 106 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 102, 105 and 106 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/16/10</u> .  | 6) <input type="checkbox"/> Other: _____                          |

Art Unit: 1654

### **DETAILED ACTION**

Applicants amendments and arguments filed 11/3/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

The original restriction requirement was sent out 7/3/06. On 3/12/07 (as noted in the office action dated 1/7/08) applicants elected group I and the species of SEQ ID NO:124.

In the instant case, the elected species is rejected under 103. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species.

Claims 1-101,103-104 have been cancelled.

Claims 102,105-106 are under consideration.

### **Information Disclosure Statement**

The information disclosure statement (IDS) submitted on 11/16/10 has been considered by the examiner.

### **Claim Rejections - 35 USC § 112**

This rejection is necessitated by applicants claim amendments.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1654

**Claims 102,105-106** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 102,105 and dependent claim 106 refer to ‘wherein the degree of inhibition of monocyte adhesion by said bioconjugate is at least five-times that of said peptide alone’.

#### Lack of Ipsis Verbis Support

The specification is void of any literal support for a range of inhibition of ‘at least five-times’.

#### Lack of Implicit or Inherent Support

Section 2163 of the MPEP states: ‘While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure’.

MPEP 2163 states:

New or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads).

Art Unit: 1654

In the instant case, the claims have been amended to recite a range of 'at least five-times'. It is noted that the phrase 'at least five-times' has no upper bound. Thus even if the specification recited there is a six-times degree of inhibition such disclosure does not necessarily represent 'at least five-times' which includes 10-times, 25-times, 1000-times, 25000-times, etc. The specification does not expressly set forth any specific degree of inhibition. Figure 4 does show data which relates to adherence (y-axis) reported as a percent of normal. It is noted that a percent of normal is not necessarily the equivalent of a degree of inhibition of at least five-times. There is no direction provided as to how to convert a percent normal difference of adherence to a degree of inhibition of adhesion. Thus from an initial inspection of the data one would not conclude that the degree of inhibition is at least five-times as recited in the claims. There is no direction provided as towards how to extrapolate or calculate the degree of inhibition from data that reports adherence as a percent of normal. It is noted that as set forth in the specification (section 0137,0138) that the standard deviation is rather large for the experimental results. For sake of argument, the average values will be compared. Section 0137 reports that the bioconjugate resulted in adherence of 3%. It would seem that the inhibition of adhesion for the bioconjugate would be the remaining fraction (i.e.  $100\% - 3\% = 97\%$ ). Section 0137 reports that the peptide alone led to an adherence of 56%. It would seem that the inhibition of adhesion for the bioconjugate would be the remaining fraction (i.e.  $100\% - 56\% = 44\%$ ). However, 97% is not at least five times 44%. There appear to be no other examples that set forth specific values for a bioconjugate and the peptide alone that would allow one to make a comparison. Thus, even if one attempts to extrapolate the data one does not arrive at the values as claimed. Thus, one

Art Unit: 1654

would not conclude that there is support for the range as instantly claimed. Hence, it can not be said that the specification provides support for the range as instantly claimed.

### **Claim Rejections - 35 USC § 103**

Claims 102,105-106 were previously rejected under 103. Since the claims have been amended the rejection is updated to correspond to the instant claims.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 102,105-106** are rejected under 35 U.S.C. 103(a) as being unpatentable over Rieu et al (Journal Cell Biology 1994 v127 pages 2081-2091 as cited in IDS 11/10/04) and Laplantine et al (Journal of Cell Science 2000 v113 pages 1167-1176; first cited with office action 5/11/09).

Art Unit: 1654

Rieu teach that the A-domain of beta2 integrin CR3 is a receptor for the hookworm-derived neutrophil adhesion inhibitor NIF (abstract). Rieu teach that integrins contain binding sites for protein ligands that play essential roles in leukocyte trafficking for example (abstract). Rieu map the NIF binding site to the A-domain and to specific peptide regions (abstract). Rieu teach (page 2086,2089) that the A-domain protein (i.e. r11bA) was immobilized and particular peptides were tested for their ability to inhibit NIF binding. One of the peptides tested (A7 figure 6) corresponded to residues 232-245 and had the amino acid sequence NAFKILVVITDGEK. Rieu teach that the binding site comprised primarily peptide A7 (page 2089 first sentence of first complete paragraph, Figure 6). Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2<sup>nd</sup> column).

Rieu does not expressly teach a peptide of SEQ ID NO:124

Rieu does teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract). Rieu teach that the A-domain may be useful for treating hookworm infections and state that the A domain is a target for anti-inflammation therapeutics (page 2090). Thus one would be motivated to identify the A-domain. Rieu also notes that certain peptides did not absorb adequately (page 2086 first paragraph last sentence). Rieu teach that numerous peptides could not be tested because the peptides did not adequately bind to plastic wells (page 2086). Thus one would be motivated to use alternative assays that allow for adequate immobilization of the peptides.

Laplantine also teach about interactions between integrins and other proteins (title, abstract). Like Rieu, Laplantine recognize that integrins play an important role in triggering

Art Unit: 1654

intracellular signaling (page 1167, page 1174). Laplantine investigate the interactions between a beta1 integrin and an alpha3 integrin (abstract). Laplantine specifically use surface plasmon resonance to investigate the interaction (page 1169 section 'surface Plasmon resonance, pages 1172-1173, Figure 7). Specifically, Laplantine teach that peptides corresponding to the beta1 subunit and containing an additional N-terminal cysteine residue were immobilized on a dextran through thiol coupling (page 1173 first column). The immobilized peptides were then exposed to peptides corresponding to alpha subunits and binding profiles were recorded (page 1173 first column).

Since Rieu teach investigating the interaction between an integrin and a possible interacting partner one would be motivated to use known techniques that are used to investigate such interactions. Since Rieu teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract) and that the A-domain may be useful for treating hookworm infections and that the A domain is a target for anti-inflammation therapeutics (page 2090) and that certain peptides did not absorb adequately (page 2086 first paragraph last sentence) one would be motivated to further study the A-domain NIF interaction. Rieu teach that numerous peptides could not be tested because the peptides did not adequately bind to plastic wells (page 2086). Since Laplantine teach surface plasmon resonance as a specific method to investigate integrin interactions one would be motivated to use the method of Laplantine with a reasonable expectation of success. Since Laplantine provide a specific example (see Figure 7) one would have a reasonable expectation of success. Laplantine teach (page 1174) that the surface plasmon resonance indicated interactions between integrin peptides and other subunit peptides. Thus one would have a reasonable expectation of success



Art Unit: 1654

that the method would be able to indicate interactions between an integrin and an interacting partner as in the peptides of Rieu.

Since Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK) (page 2089 first sentence of first complete paragraph, Figure 6) one would be motivated to use such peptide as the sequence to attach to the dextran. Since Laplantine teach that the dextran is attached via thiol coupling to an additional N-terminal cysteine residue (page 1173 first column) one would be motivated to add an N-terminal cysteine to peptide A7 of Rieu to obtain CNAFKILVVITDGEK and then couple the dextran. The resulting product would be the peptide CNAFKILVVITDGEK (which is SEQ ID NO:124 of the instant invention) covalently attached by thiol coupling to a dextran thus meeting the limitations of claims 102,105-106 of the instant invention.

It is noted that the instant claims recite 'bioconjugate consisting of'...'having'. In the instant case, the conjugate obviated by the prior art (i.e. the peptide CNAFKILVVITDGEK covalently attached by thiol coupling to a dextran) meets the claim limitations. Further, it is noted that section 2111.03 of the MPEP discusses transitional phrases (see *In re Crish*, 393 F.3d 1253, 73 USPQ2d 1364 (Fed. Cir. 2004)).

It is noted that claims 102,105 recite 'that inhibits inflammatory...'. Rieu teach that the A-domain plays an essential role in trafficking to inflammatory sites (abstract). It is noted that claims 102 and 105 recite wherein clauses that recite functional properties of the claimed product. In the instant case, the prior art expressly teach the hydrophilic polymer/polysaccharide as recited in claim 106. Thus there is a reasonable basis that the polysaccharide has the recited function. Further, the prior art suggest the peptide sequence as recited in claims 102,105. Thus

Art Unit: 1654

there is a reasonable basis that the peptide has the recited function. It is noted that prior art suggests applicants elected species. Thus there is a reasonable basis that such species would function as claimed. Rieu teach the A-domain as a receptor for adhesion inhibitors (title).

In the instant case, both Rieu and Laplantine are drawn to methods of identifying interacting regions between integrins and interaction partners. Rieu teach a method in which peptides were adsorbed to plastic wells but notes that numerous peptides did not absorb adequately (page 2086 first paragraph). Laplantine teach a method in which selected peptides containing an additional N-terminal cysteine were immobilized on dextran through thiol coupling and used as part of a surface plasmon resonance analysis. The claims would have been obvious because a particular known technique (i.e. surface plasmon resonance) was recognized as part of the ordinary capabilities of one skilled in the art. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

### **Response to Arguments 103 rejection**

Applicants argue (pages 3-8) that the claim preamble has been amended to recite 'that inhibits inflammatory cell adhesion' and the preamble provides a definition of the invention's limitations and that the claim has been amended to recite a wherein clause and that the art does not teach that the hydrophilic polymer inhibits monocyte adhesion to the cell.

Applicants argue that no motivation is provided to cross-link the peptide to a polysaccharide and Applicants argue that there is no more than an invitation to try.

Applicants argue that the nature of the problem to be solved was not to test direct binding but to inhibit inflammatory cell adhesion and that one would not have an expectation of success of inhibiting adhesion as claimed.

Applicants argue that the composition of Laplantine included a sensor chip that is not included in the claimed invention.

Applicants argue that there is no suggestion that the dextran will inhibit adhesion and that the bioconjugate shows unexpected and synergistic activity as evidenced in Figure 4 and the text.

Applicant's arguments filed 11/3/10 have been fully considered but they are not persuasive.

Although Applicants argue (pages 3-8) that the claim preamble has been amended to recite 'that inhibits inflammatory cell adhesion' and the preamble provides a definition of the invention's limitations and that the claim has been amended to recite a wherein clause and that the art does not teach that the hydrophilic polymer inhibits monocyte adhesion to the cell, MPEP 2111.02 states: 'During examination, statements in the preamble reciting the purpose or intended use of the claimed invention must be evaluated to determine whether the recited purpose or intended use results in a structural difference'. In the instant case the claims use the closed language 'consisting of'. Thus, there is no basis to assert that an unclaimed component is required for the recited function. Since the prior art suggest the claimed elements specifically applicants elected species of peptide and the polysaccharide as recited in claim 106 there is a reasonable basis that the claim limitations are met. The instant claims are drawn to products and

Art Unit: 1654

the claims set forth the components of the product. Applicants elected species as recited in claims 102,105 recite a specific peptide and claim 106 recites a specific dextran. Since the prior art suggest such components there is a reasonable basis that the claim limitations are met. It would seem inconsistent with applicants disclosure to assert that the recited components do not act as claimed. With respect to the wherein clause MPEP 2111.04 states that claim scope is not limited by claim language that does not limit a claim to a particular structure. Applicants elected species as recited in claims 102,105 recite a specific peptide and claim 106 recites a specific dextran so there is a reasonable basis that such structures meet the claim limitations. Since the prior art suggest such components there is a reasonable basis that the claim limitations are met. Rieu teach that the A-domain plays an essential role in trafficking to inflammatory sites (abstract). Rieu teach the A-domain as a receptor for adhesion inhibitors (title).

Although Applicants argue that no motivation is provided to cross-link the peptide to a polysaccharide and Applicants argue that there is no more than an invitation to try, as stated in the rejection since Rieu teach investigating the interaction between an integrin and a possible interacting partner one would be motivated to use known techniques that are used to investigate such interactions. Since Rieu teach that identification of the region in NIF mediating A-domain binding should be useful to understanding physiological functions (abstract) and that the A-domain may be useful for treating hookworm infections and that the A domain is a target for anti-inflammation therapeutics (page 2090) and that certain peptides did not absorb adequately (page 2086 first paragraph last sentence) one would be motivated to further study the A-domain NIF interaction. Rieu teach that numerous peptides could not be tested because the peptides did not adequately bind to plastic wells (page 2086). Since Laplantine teach surface plasmon

Art Unit: 1654

resonance as a specific method to investigate integrin interactions one would be motivated to use the method of Laplantine with a reasonable expectation of success. Since Laplantine provide a specific example (see Figure 7) one would have a reasonable expectation of success. Laplantine teach (page 1174) that the surface plasmon resonance indicated interactions between integrin peptides and other subunit peptides. Thus one would have a reasonable expectation of success that the method would be able to indicate interactions between an integrin and an interacting partner as in the peptides of Rieu. Rieu teach that the A-domain may be useful for treating hookworm infections and state that the A domain is a target for anti-inflammation therapeutics (page 2090). Importantly, Rieu teach that specific peptide fragments were assayed (figure 6). One of the peptides tested (A7 figure 6) corresponded to residues 232-245 and had the amino acid sequence NAFKILVVITDGEK. Rieu teach that the binding site comprised primarily peptide A7 (page 2089 first sentence of first complete paragraph, Figure 6). Rieu teach that the A7 peptide has previously been found to bind to iC3b (page 2089 2<sup>nd</sup> column). Rieu teach that the binding site comprised primarily peptide A7 (i.e. NAFKILVVITDGEK). Thus Rieu teach a specific peptide fragment from a specific protein. Rieu teach that the A-domain may be useful for treating hookworm infections and state that the A domain is a target for anti-inflammation therapeutics (page 2090). Thus one would be motivated to identify the A-domain. Since the experiments of Rieu were limited by the inability of certain peptides to bind one would be motivated to use other known methods to test direct binding. As discussed above, Laplantine teach such methods. One would have been motivated to combine the references to address the problem. Thus one would be motivated to address the problem set forth in Rieu. In fact, section 2143.01 of the MPEP states: "The court found motivation to combine the references to arrive at

Art Unit: 1654

the claimed invention in the “nature of the problem to be solved” because each reference was directed “to precisely the same problem of underpinning slumping foundations.” Id. at 1276, 69 USPQ2d at 1690. The court also rejected the notion that “an express written motivation to combine must appear in prior art references....” Id. at 1276, 69 USPQ2d at 1690.” Further, section 2143.03 of the MPEP states: “person of ordinary skill in the art is also a person of ordinary creativity, not an automaton.” KSR International Co. v. Teleflex Inc., 550 U.S. \_\_\_, \_\_\_, 82 USPQ2d 1385, 1397 (2007). “[I]n many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle.” Id. Office personnel may also take into account “the inferences and creative steps that a person of ordinary skill in the art would employ.” Id. at \_\_\_, 82 USPQ2d at 1396.”

Although Applicants argue that the nature of the problem to be solved was not to test direct binding but to inhibit inflammatory cell adhesion and that one would not have an expectation of success of inhibiting adhesion as claimed, MPEP 2144IV (see also MPEP 2145 II) expressly state that the reason or motivation to modify the reference may include a different rationale from applicants. With regards to an expectation of success, it is noted that Laplantine sets forth a known method (Laplantine specifically use surface plasmon resonance to investigate the interaction (page 11169 section ‘surface Plasmon resonance, pages 1172-1173, Figure 7)) using known synthesis strategies (Laplantine teach that peptides corresponding to the beta1 subunit and containing an additional N-terminal cysteine residue were immobilized on a dextran through thiol coupling (page 1173 first column)). Since Laplantine teach surface plasmon resonance as a specific method to investigate integrin interactions one would be motivated to use the method of Laplantine with a reasonable expectation of success. Since Laplantine provide a

Art Unit: 1654

specific example (see Figure 7) one would have a reasonable expectation of success. Laplantine teach (page 1174) that the surface plasmon resonance indicated interactions between integrin peptides and other subunit peptides. Thus one would have a reasonable expectation of success that the method would be able to indicate interactions between an integrin and an interacting partner as in the peptides of Rieu.

Although Applicants argue that the composition of Laplantine included a sensor chip that is not included in the claimed invention, it is noted that claim 102 refers to a 'hydrophobic polymer', claim 105 refers to 'polysaccharide' and claim 106 recites 'dextran'. Laplantine expressly recite that the chip was a carboxymethyldextran chip (page 1169 section 'surface plasmon resonance'). Thus Laplantine teach that the chip was carboxymethyldextran. MPEP 2145 I states that attorney argument cannot take the place of evidence in the record. There is no evidence of record to show that the chip contains anything other than carboxymethyldextran since Laplantine expressly recite that the chip was a carboxymethyldextran chip (page 1169 section 'surface plasmon resonance'). Whether or not the carboxymethyldextran is in the form of a chip does not discredit that it is a type of dextran.

Although Applicants argue that there is no suggestion that the dextran will inhibit adhesion and that the bioconjugate shows unexpected and synergistic activity as evidenced in Figure 4 and the text, MPEP 716.02(a) states that synergism involves demonstration of an effect which is greater than each of the effects taken separately. With respect to figure 4, it is noted that as set forth in the specification (section 0137,0138) that the standard deviation is rather large for the experimental results. From a simplistic analysis of Figure 4 (ignoring the large error bars) it appears that dextran alone and peptide alone have about half the value (decrease of ~50%) of the

Art Unit: 1654

positive control. The dextran/peptide combination has a value near zero. Thus it appears that the results are additive (decrease of ~50% + decrease of ~50% = decrease of ~100%). A closer inspection reveals that the adherence (percent of normal) for the dextran alone is  $55.65 \pm 23.42\%$  (note that  $55.65 + 23.42 = 79.07$  and  $55.65 - 23.42 = 32.23$ ). The adherence for the peptide alone is  $56.28 \pm 22.67\%$ . The adherence of the peptide/dextran is  $3.34 \pm 1.69\%$ . Although applicants refer to inhibition of adhesion, such variable is not reported in Figure 4 nor is the standard deviation reported for the inhibition of adhesion. MPEP 716.02(b) states that the burden is on the applicant to establish that results are unexpected. There is no direction provided as towards how to extrapolate or calculate the degree of inhibition from data that reports adherence as a percent of normal. For sake of argument, it would seem that the inhibition of adhesion for the bioconjugate would be the remaining fraction (i.e.  $100\% - \text{adherence}\%$ ) of the value reported. For the dextran alone the value is  $(100 - 55.65) \pm 23.42\% = 44.35 \pm 23.42\%$ . For the peptide alone the value is  $(100 - 56.28) \pm 22.67\% = 43.72 \pm 22.67\%$ . For the combination  $(100 - 3.34) = 96.66$  (simply ignoring the error bars). Thus one would expect a combination of the peptide and dextran to result in  $(44.35 + 43.72) \pm ((23.42 + 22.67)/2)\% = 88.07 \pm 23.05$ . Thus the actual value (96.66) is within the expected range ( $88.07 \pm 23.05$ ). Therefore, there is no basis to conclude that the results are synergistic.

With respect to the assertion of unexpected results, it is first noted that MPEP 716.02(d) states that unexpected results are to be commensurate in scope with the claimed invention. Figure 4 reports data related to dextran while claims 102, 105 are much broader than dextran. Further, the relevant question is whether or not there is an expectation for dextran to inhibit as



Art Unit: 1654

claimed (see MPEP 716.02(b)). It is noted that MPEP 716.02(c) II states that expected beneficial results are evidence of obviousness.

Roufa et al (US 6,417,173) teach dextrans to inhibit adhesions (abstract). Roufa teach (claims 1,6,14,36,45) inhibiting monocytes using polymers, specifically a dextran. Thus there is a reasonable basis to expect dextrans to inhibit monocytes.

Bremerskov V ('Dextran sulphate inhibits cell adhesion in tissue culture' Nature New Biology v246 Dec 12 1973, page 174) teach that dextran sulphate inhibits cell adhesion (title). Thus there is a reasonable basis to expect dextrans to inhibit cell adhesion.

Krivan et al ('Adhesion of Mycoplasma pneumoniae to sulfated glycolipids and inhibition by dextran sulfate' Journal of Biological Chemistry v264 June 5 1989 pages 9283-9288) teach that dextran sulfate inhibits cell adhesion (abstract). Thus there is a reasonable basis to expect dextrans to inhibit cell adhesion.

Matsumiya et al ('Dextran sulfate inhibits e-selectin-mediated neutrophil adhesion to endotoxin-activated vascular endothelial cells' Life Sciences v64 1999 pages 9-17) teach that dextran sulphate inhibits neutrophil adhesion (abstract). Thus there is a reasonable basis to expect dextrans to inhibit inflammatory cell adhesion.

Thus the prior art is evidence of an expected beneficial result (dextran inhibits cell adhesion).

### **Prior art of record**

The prior art previously made of record (5/11/09) and not relied upon is considered pertinent to applicant's disclosure:

Art Unit: 1654

Arnaut WO 91/19511: Arnaut teach SEQ ID NO:50 (comprises NAFKILVVITDGEK) (see claim 5 for example) and carriers for administering the peptides (claim 17).

Bocher et al (Journal of Immunological Methods 1997 v208 pages 191-202). Bocher teach the use of peptide-dextran conjugates compared to the use of peptide adsorbed onto immunoplates (abstract).

### **Conclusion**

In the instant case, applicants amendments have necessitated any new grounds of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Art Unit: 1654

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/  
Examiner, Art Unit 1654

/Cecilia Tsang/  
Supervisory Patent Examiner, Art Unit 1654